

MODULE 2

Feeding Centres in the Brain- Hypothalamus

The hypothalamus is a region of the brain that plays a critical role in feeding regulation.

It is also responsible for the control of hunger and thirst.

In the basal hypothalamus there are several nuclei that regulate and control the appetite.

There are “orexigenic and anorexigenic neurotransmitters” in the hypothalamus. The orexigenic neurotransmitters increase appetite while the anorexigenic ones decrease appetite.

Parts of the hypothalamus related to appetite

Some parts of the hypothalamus are related to appetite. These include:

1. **The Arcuate nucleus** – The arcuate nucleus (ARC) is located at the base of the hypothalamus. This has a high density of neurons that produce the orexigenic peptides, NPY (Neuropeptide Y), the opioids, endorphin, amino acids, γ -aminobutyric acid and glutamate.
2. **Ventromedial nucleus and lateral hypothalamus** – It has been seen that any lesion in these areas leads to excessive appetite, and abnormal body weight gain that persist for a long time. These sites are said to possess a “satiety center” that constantly increases the feeding behaviour.
3. **Paraventricular nucleus and perifornical hypothalamus** – This region has neuronal elements that control ingestive behavior. When injected with orexigenic signals, GABA, opioids, norepinephrine (NE), and epinephrine (E) this region is activated and leads to increased food intake. If injected with anorexigenic signals like CRH and leptin, this region leads to lowered feeding.

4. **Dorsomedial nucleus** – These areas when injected with orexigenic signals lead to excessive feeding. But no effect for anorexigenic signals.
5. **Suprachiasmatic nucleus** - The drive to eat is evoked by appetite or the sensation of hunger. This is based on the perception of the light-dark cycle. For example, rats consume between 85–90% of their total intake during dark periods. In humans signalling of appetite is linked to individual based requirements. These include neural, metabolic, and hormonal signals that tell a person it's time to eat.

Internal cues for Feeding:

1. Glucose based signal:

To stay alive, our cells must be supplied with fuel and oxygen. Obviously, fuel comes from the digestive tract, as a result of eating.

But the digestive tract is sometimes empty; in fact, most of us wake up in the morning in that condition. So there has to be a reservoir that stores nutrients to keep the cells of the body nourished when the gut is empty. Indeed, there are two reservoirs: one short term and the other long-term. The short-term reservoir stores carbohydrates, and the long-term reservoir stores fats.

The short-term reservoir is located in the cells of the liver and the muscles, and it is filled with a complex, insoluble carbohydrate called glycogen. Cells in the liver convert glucose (a simple, soluble carbohydrate) into glycogen and store the glycogen, by the presence of insulin, a peptide hormone produced by the pancreas. Thus, when glucose and insulin are present in the blood, some of the glucose is used as a fuel, and some of it is stored as glycogen. Later, when all of the food has been absorbed from the digestive tract, the level of glucose in the blood begins to fall.

The fall in glucose is detected by cells in the pancreas and in the brain. The pancreas responds by stopping its secretion of insulin and starting to secrete a different peptide hormone: glucagon. The effect of

glucagon is opposite that of insulin: It stimulates the conversion of glycogen into glucose.

Thus, the liver soaks up excess glucose and stores it as glycogen when plenty of glucose is available, and it releases glucose from its reservoir when the digestive tract becomes empty and the level of glucose in the blood begins to fall.

2.Fat based signal:

Our long-term reservoir consists of adipose tissue (fat tissue). This reservoir is filled with fats, or, more precisely, with triglycerides. Triglycerides are complex molecules that contain glycerol combined with three fatty acids. Adipose tissue is found just beneath the skin and in various locations in the abdominal cavity.

It consists of cells that are capable of absorbing nutrients from the blood, converting them to triglycerides. These cells can expand enormously in size. The primary physical difference between an obese person and a person of normal weight is determined by the size of their fat cells and the amount of triglycerides that these cells contain.

The long-term fat reservoir will keep us alive when we are fasting. When the digestive system is empty, there is an increase in the activity of the adipose tissue, the pancreas, and the adrenal medulla. It causes the secretion of glucagon, and secretion of adrenal hormones. Thus, the long-term fat reservoir to be broken down into glycerol and fatty acids. The fatty acids can be directly metabolized by cells in all of the body except the brain, which needs glucose.

Palatability: Role of Opioids:

The palatability of a substance is determined by opioid receptor-related processes in the nucleus accumbens and ventral pallidum. This area has been called the "opioid eating site"

Opioids are any compounds that resemble the naturally occurring alkaloids found in the resin of the opium poppy.

Opioid agonists(increase) and antagonists have corresponding **stimulatory and inhibitory effects on feeding**.

Studies with the consumption of palatable fluids also indicate a role for opioids in **taste reward**.

A substantial amount of scientific evidence demonstrates that the action of various opioids is a major contributor to both the motivation to seek food and the pleasure of consuming food.

opioid palatability hypothesis which states that opioids modulate feeding behaviors via the stimulation of an increased perception of food palatability.

This can be seen very distinctly in laboratory animals following direct injection of morphine or opioid antagonists into the hypothalamus. Morphine injection induces hyperphagia, whereas, opioid antagonists' injection results in significant reductions in food intake, proves **stimulatory and inhibitory effects on feeding**.

Role of GABA

Several lines of study have suggested that GABA in the hypothalamic feeding center plays a role in **promoting food intake**. Recent studies revealed that the NPY/AGRP neurons in the hypothalamic arcuate nucleus (ARC) are the feeding centres in brain.

GABA and GABAergic neurons also act as an orexigenic centre in brain.

GABA stimulates the hypothalamic GABA receptors, increases food intake and body weight. GABA supplements also causes a reduction in body fat and triglyceride levels while increasing lean muscle mass.

Taste Aversion

Taste Aversion- the mind develops a **resistance towards a certain food**. Eating certain types of food can cause a bad reaction.

This is a form of classical condition when the body uses a natural instinct as a means of protection. This is also called a survival mechanism. It warns the body if a type of food (berries or mushrooms) is harmful. When people have a bad experience with spoiled or toxic food, they can develop a taste aversion.

Taste aversion is a learned response to eating spoiled or toxic food. When taste aversion takes place, you avoid eating the foods that make you ill.

Abnormalities of Feeding:

1. Excessive food craving:

People might experience food cravings seemingly out of nowhere, or they may be related to seeing, smelling, or hearing about a specific food. For instance, seeing an advertisement for chocolate might trigger a craving for it.

The brain regions responsible for memory, pleasure, and reward play a role in food cravings. An imbalance of hormones, such as leptin and serotonin, could also lead to food cravings.

Cravings also involve the appetite centers of the brain, even though they tend to be separate from hunger.

There are two types of food cravings: selective and nonselective.

Selective cravings are cravings for specific foods, such as a person's favorite chocolate bar, a particular burger from their favorite restaurant, or a bag of potato chips of a certain flavor.

Nonselective hunger is the desire to eat anything. It may be the result of real hunger and hunger pangs, but it can also be a sign of thirst. Drinking water may help with intense nonselective cravings.

Physical causes

- Leptin and ghrelin imbalances.
- Pregnancy.
- Premenstrual syndrome (PMS).
- Lack of sleep.
- A nutrient-poor diet.
- Poor hydration
- Your gut flora.
- Physical activity.
- Highly processed foods.
- Frequency at which you eat the craved foods.

2. Obesity

Obesity is a complex disease that occurs when an individual's weight is higher than what is considered healthy for his or her height. Obesity affects children as well as adults. Many factors can contribute to excess weight gain including eating patterns, physical activity levels, and sleep routines. Social determinants of health, genetics, and taking certain medications also play a role.

Health risks of Obesity

- Type 2 diabetes
- High blood pressure
- Heart disease
- Stroke
- Sleep apnea
- Fatty liver diseases
- Osteoarthritis
- Gallbladder diseases
- Some cancers
- Kidney disease
- Pregnancy problems (gestational diabetes)

Anorexia nervosa

Often simply called anorexia — is an eating disorder characterized by an abnormally low body weight, an intense fear of gaining weight. People with anorexia have a high value on controlling their weight and shape.

To prevent weight gain or to continue losing weight, people with anorexia usually severely restrict the amount of food they eat. They may control calorie intake by vomiting after eating or by misusing diet aids. They may also try to lose weight by exercising excessively.

Physical symptoms

- Extreme weight loss
- Thin appearance
- Abnormal blood counts
- Fatigue
- Insomnia
- Dizziness or fainting
- Bluish discoloration of the fingers
- Hair that thins, breaks or falls out
- Soft, downy hair covering the body
- Absence of menstruation
- Constipation and abdominal pain
- Dry or yellowish skin
- Intolerance of cold
- Irregular heart rhythms
- Low blood pressure
- Dehydration
- Swelling of arms or legs
- Eroded teeth

A combination of biological, psychological and environmental factors are the reasons:

- **Biological.** There may be genetic changes that make some people at higher risk of developing anorexia.
- **Psychological.** Some people with anorexia may have obsessive-compulsive personality traits. They may have an extreme drive for perfectionism, which causes them to think they're never thin enough. And they may have high levels of anxiety.
- **Environmental.** Modern Western culture emphasizes thinness. Peer pressure may help fuel the desire to be thin, particularly among young girls.

Prevention

There's no guaranteed way to prevent anorexia nervosa. Primary care by a physician can be helpful.

Cancer associated Anorexia:

Most people with advanced cancer have some degree of anorexia. Decreased nutrition due to appetite changes can lead to weight loss, malnutrition, loss of muscle mass. oncologists are increasingly addressing the role of nutrition in cancer patients by knowing the effect of poor nutrition on treatment response.

symptoms related to cancer or treatment can add to poor appetite”

- Mouth sores
- Taste changes
- Fatigue
- Depression
- Nausea or vomiting
- Difficulty swallowing (dysphagia)
- Shortness of breath
- Pain
- Medications:

Treatment:

- Medication to stimulate your appetite.

- Artificial Nutrition
- Complimentary/alternative therapies (such as herbal supplements and meditation)

Neural And Hormonal Mechanism of Eating: The Arcuate Nucleus & Feeding Behavior:

The **arcuate nucleus** of the hypothalamus also known as **ARH, ARC**, or **infundibular nucleus** is an aggregation of neurons in the medio basal hypothalamus

The arcuate nucleus provides many physiological roles involved in feeding, metabolism, fertility, and cardiovascular regulation.

The **arcuate nucleus** is a small part of the hypothalamus that plays an extremely important role in the regulation of hormone secretion from the pituitary gland, and in the regulation of appetite and body weight.

The arcuate nucleus has a key role in the regulation of feeding behaviour, through two important populations of centrally projecting neurons:

- Neurons that contain **Neuropeptide Y (NPY)**; another peptide, **Agouti-Related Protein (AGRP)**; and the inhibitory neurotransmitter **GABA**.
- These neurons, project strongly to the lateral hypothalamus and are important in the regulation of appetite
- NPY and AGRP are both very potent stimulators of feeding behaviour.
- The expression of NPY and AGRP is strongly increased after a period of fasting, and when activated, these neurons can produce voracious eating when food is available.
- These neurons are regulated by circulating concentrations of leptin (a hormone secreted from fat cells (adipose tissue) and ghrelin (a hormone secreted from the stomach when it is empty).

The orbitofrontal cortex (OFC) & Feeding Behavior:

The orbitofrontal cortex (OFC) is a prefrontal cortex region in the frontal lobes of the brain which is involved in the cognitive process of decision-making.

The lateral orbitofrontal cortex (LOFC) receives sensory information about food and integrates these signals.

This play a key role in a distributed network of neural circuits that regulate feeding behavior.

It receives and integrates inputs from all the sensory modalities: taste, smell.

The OFC may be anatomically and functionally situated to play a critical role in the maintenance of excess feeding behaviour.

Neuropeptide Y & Feeding Behavior:

Neuropeptide Y (NPY) A peptide neurotransmitter found in a system of neurons of the Arcuate nucleus.

The Functions of NPY are:

- stimulate feeding,
- Insulin secretion,
- glucocorticoid secretion;
- Decrease the breakdown of triglycerides
- Decrease body temperature.

Insulin & Feeding Behavior:

Insulin is a pancreatic hormone that facilitates entry of glucose and amino acids into the cell.

Functions of Insulin:

- Conversion of glucose into glycogen,
- Transport of fats into adipose tissue.

Melanocyte-Stimulating Hormone (MSH) & Feeding Behavior:

Melanocyte-stimulating hormone refers to a group of peptide hormones released by the pituitary gland and hypothalamus.

By acting on receptors in the hypothalamus, melanocyte-stimulating hormone, suppress appetite.

Melanocyte-Stimulating Hormone (MSH) A neuropeptide that acts as an agonist (binding molecule) to hypothalamus and inhibits eating.

Hunger satiety -Determinants of Satiety

Satiety is the feeling of fullness after a meal. A **satiating meal** will make you feel full with less energy and stop you from feeling hungry for longer.

Combined mechano- and chemoreceptors, peripherally released peptide hormones and neural pathways provide feedback to the brain to determine sensations of hunger (increase energy intake) or satiation (termination of energy intake) and regulate the human metabolism.

The gastric filling reflex, which consists of a relaxation of the stomach during food intake, has been identified as a major determinant of meal volume, through activation of tension-sensitive gastric mechanoreceptors.

Hormones determining satiety:

In addition, the release of several peptide hormones such as glucagon-like peptide 1 (GLP-1), cholecystokinin as well as motilin and ghrelin contribute to gut-brain signalling with relevance to control of hunger and satiety.

A number of nutrients, such as bitter tastants, as well as pharmacological agents, such as endocannabinoids influence hunger, satiation and food intake.

The release of **Motilin**, is the trigger of gastric Phase 3, has been identified as the major determinant of return of hunger after a meal.

Cholecystokinin is hormone that stimulates satiety and is secreted from the gastrointestinal tract.

It is the most recognised functions of this hormone are in digestion and appetite. It improves digestion by slowing down the emptying of food from the stomach and stimulating the production of bile in the liver as well as its release from the gall bladder.

The type and amount of food we eat can stimulate appetite.

Secretion gut hormones affect the brain and behavior. The two most famous hormones involved in regulating hunger and satiety are ghrelin and leptin.

Leptin is a satiety hormone secreted from the pancreas. The type and amount of food you eat can stimulate appetite.

Secretion gut hormones affect the brain and behavior. The stomach secretes ghrelin when the body needs caloric energy.

Leptin is a mediator of long-term regulation of energy balance, suppressing food intake and thereby inducing weight loss.

The most significant driver of leptin production is your total body fat level. The more body fat an individual has, the more leptin in blood circulation.

The ghrelin Is a hormone secreted by stomach when the body needs caloric energy.

Ghrelin is a hormone produced by the gastrointestinal tract, especially the stomach, and is called a "hunger hormone" because it increases the drive to eat.

Blood levels of ghrelin are highest before meals when hungry, returning to lower levels after mealtimes

Ghrelin may help prepare for food intake by increasing gastric motility and stimulating the secretion of gastric acid.

Brain regions determining Satiety:

The lateral hypothalamus, on the orbitofrontal cortex, and by modulating sensory activity to set the pleasantness and reward value of food.

The outputs of the orbitofrontal cortex then reach brain regions such as the striatum, cingulate cortex, and dorsolateral prefrontal cortex, where behavioral responses to food may be elicited

At the same time, outputs from the orbitofrontal cortex and amygdala, may provide appropriate autonomic and endocrine responses to food including the release of hormones such as insulin.